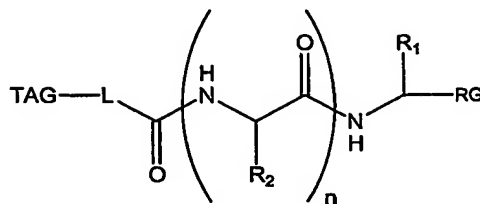


Claims

1. An activity based probe having the structure,



wherein

each R_1 and R_2 is independently hydrogen or C_{1-6} alkyl, straight or branched chain, optionally containing from 1-3 heteroatoms selected from the group consisting of N, O, or S, or C_{0-6} alkyl aryl, C_{0-6} alkyl heteroaryl, or C_{0-6} alkyl phenyl;

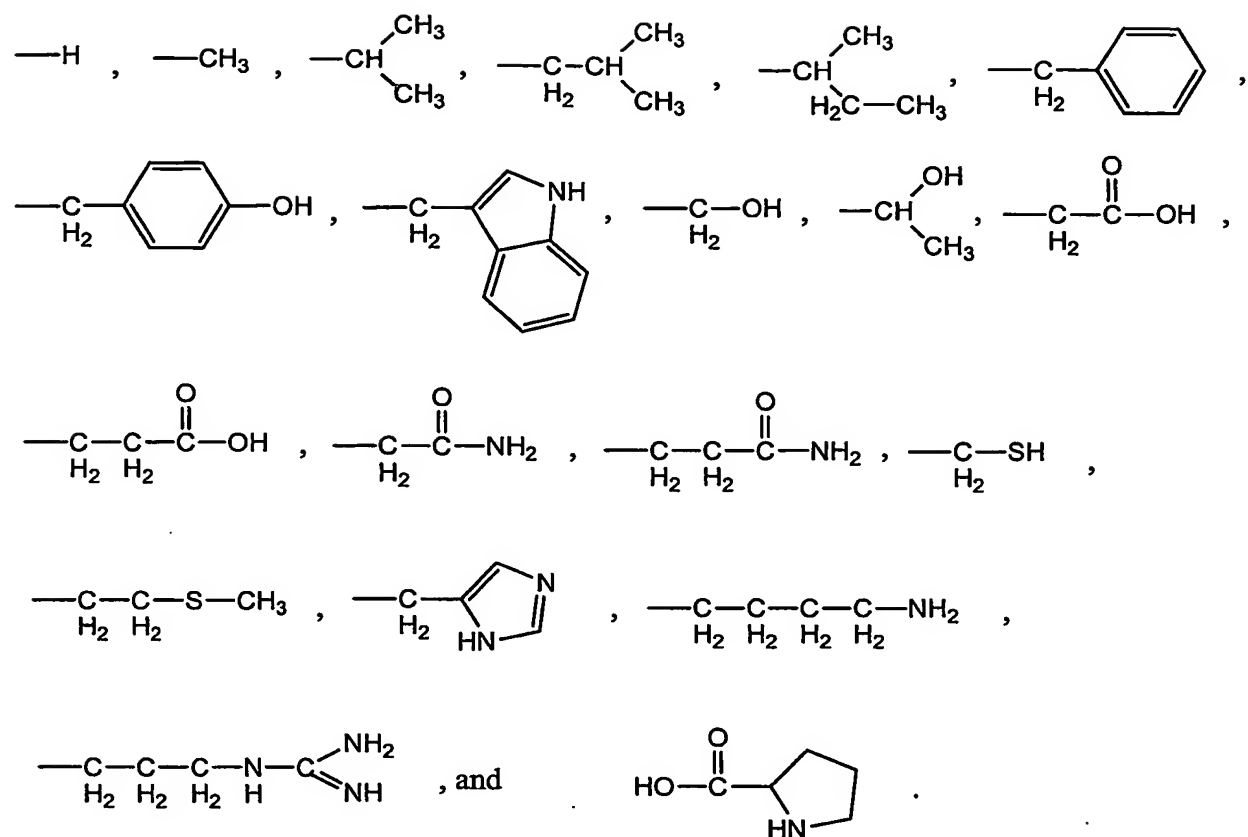
RG is a reactive group that reacts to form a covalent bond with a catalytically active target enzyme;

L is optionally present and is an alkyl or heteroalkyl group of 1-20 backbone atoms selected from the group consisting of: $-\text{N}(\text{R})-$, $-\text{O}-$, $-\text{S}-$ or $-\text{C}(\text{R})(\text{R})-$, where each R is independently H or a $-\text{C}_{1-6}$ alkyl straight or branched chain;

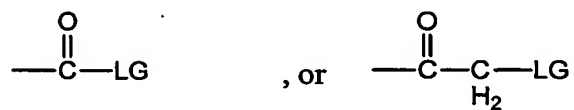
n is an integer from 1 to 4;

or a pharmaceutically acceptable salt or complex thereof.

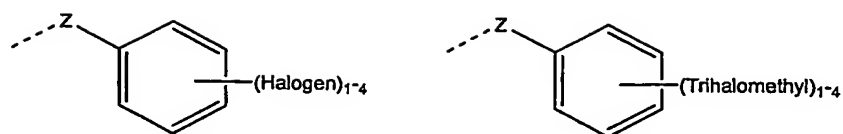
2. An activity based probe of claim 1 wherein n is 1 or 2.
3. An activity based probe of claim 1, wherein each R_1 and R_2 are independently selected from the group consisting of



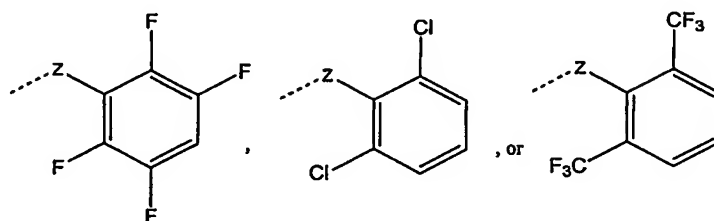
4. An activity based probe of claim 1, wherein RG is selected from the group consisting of



wherein LG is selected from the group consisting of

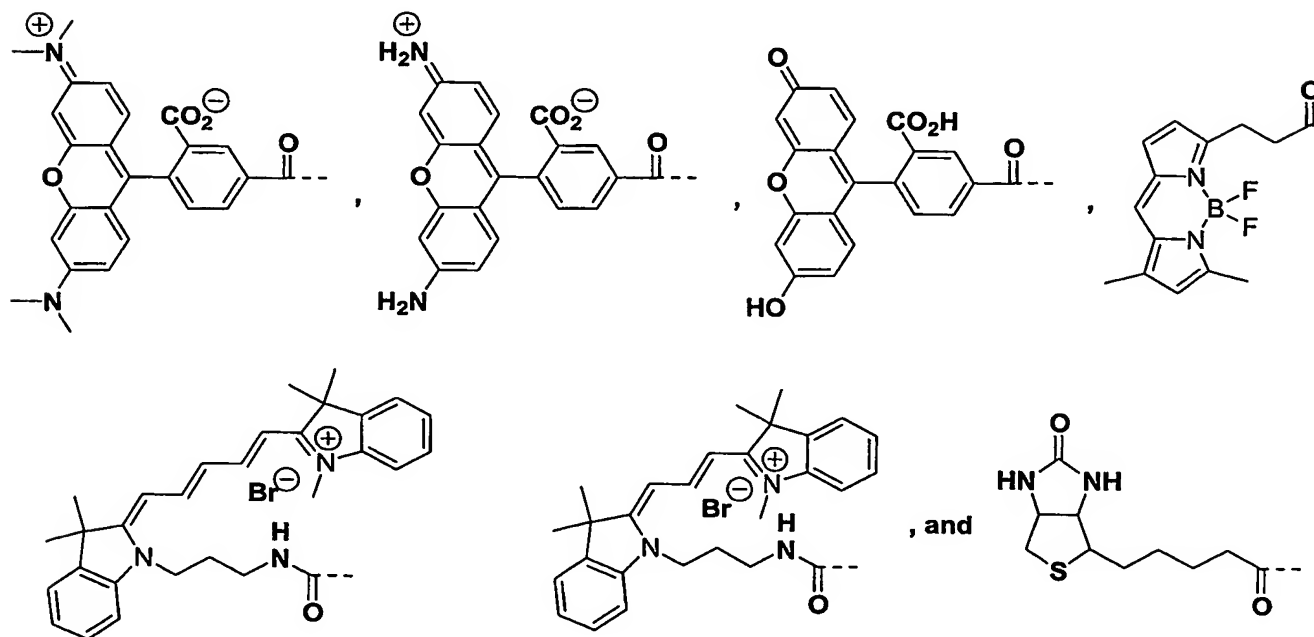


5. An activity based probe of claim 4 wherein LG is selected from the group consisting

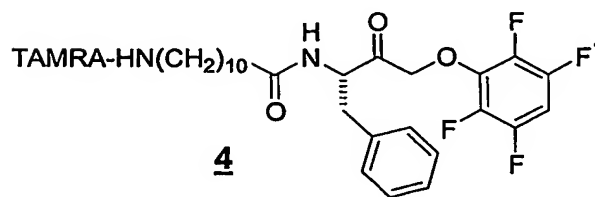
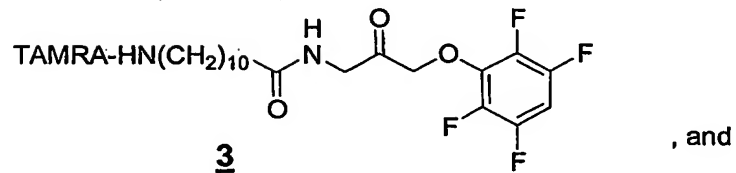
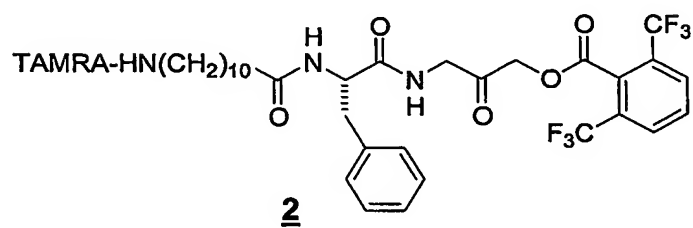
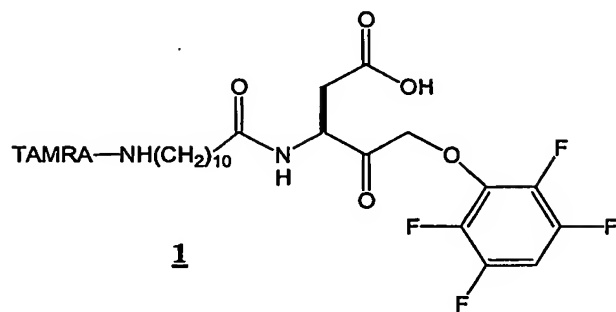


of:

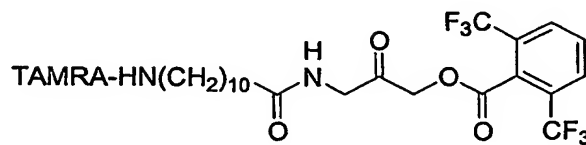
6. An activity based probe of claim 1 wherein TAG is selected from the group consisting of:



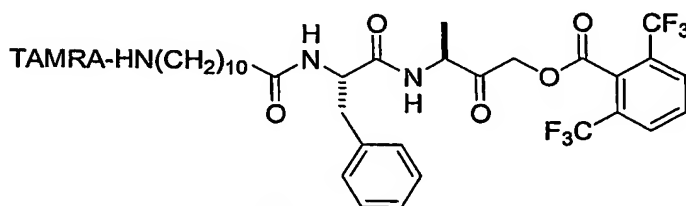
7. An activity based probe having a structure selected from the group consisting of:



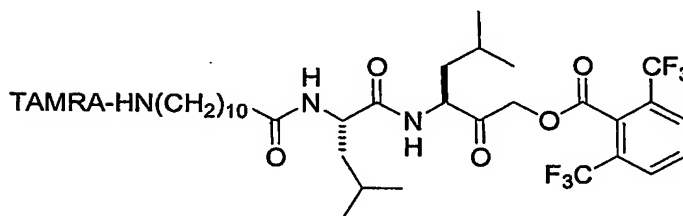
8. An activity based probe having a structure selected from the group consisting of:



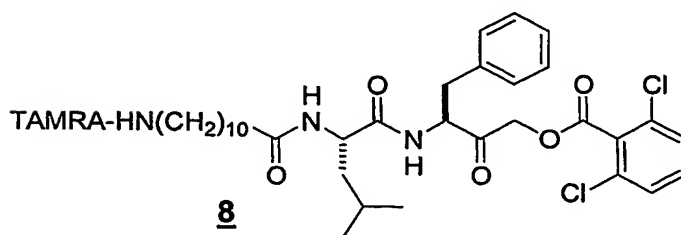
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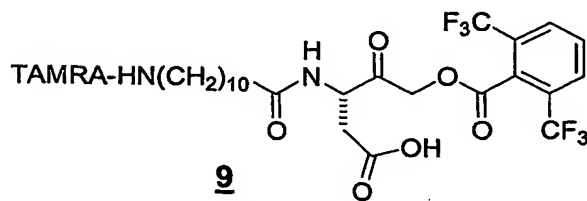


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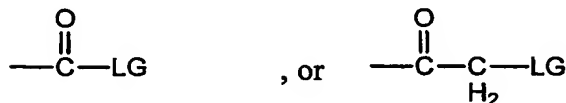
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, and

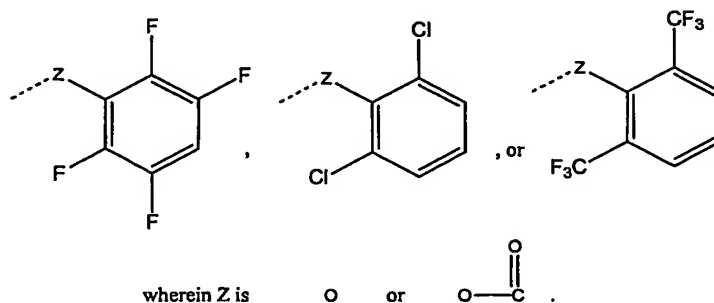


9

9. An activity based probe library comprising a plurality of activity based probe(s) of one of claims 1-8.
10. A method for determining the enzyme profile of one or more target enzymes in a complex protein mixture, employing one or more activity based probes covalently attached to a TAG through a linking moiety, and a reactive group that reacts with an amino acid functionality of said target enzyme(s) when said activity based probe(s) is(are) bound to said target enzyme(s), said method comprising:
- combining in a reaction medium said activity based probe(s) and said complex protein mixture under conditions of reaction of said activity based probe(s) with said target enzyme(s), whereby a conjugate of said activity based probe(s) and said target enzyme(s) is formed; and
- determining said enzyme profile by generating a signal from one or more conjugates formed thereby;
- wherein said activity based probe(s) are selected from the activity based probe(s) of one of claims 1-8.
11. A method according to Claim 10, wherein said reactive group is selected from the group consisting of



wherein LG has a structure selected from the group consisting of



12. A method according to Claim 10, wherein said activity based probe(s) specifically bind(s) to a one or more cysteine proteases.